Express Mail Label No. **EJ056023095US**

UTILITY PATENT APPLICATION TRANSMITTAL
(Small Entity)

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Docket No. **CRYO/US-24**
Total Pages in this Submission **27**

TO THE ASSISTANT COMMISSIONER FOR PATENTS
Box Patent Application
Washington, D.C. 20231

Transmitted herewith for filing under 35 U.S.C. 111(a) and 37 C.F.R. 1.53(b) is a new utility patent application for an invention entitled:

PRECOOLED CRYOGENIC ABLATION SYSTEM

and invented by:

Hong Li

If a CONTINUATION APPLICATION, *check appropriate box and supply the requisite information:*

☐ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: _____

Which is a:

☐ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: _____

Which is a:

☐ **Continuation** ☐ **Divisional** ☐ **Continuation-in-part (CIP)** of prior application No.: _____

Enclosed are:

Application Elements

1. ☒ Filing fee as calculated and transmitted as described below
2. ☒ Specification having **14** pages and including the following:
   a. ☒ Descriptive Title of the Invention
   b. ☐ Cross References to Related Applications *(if applicable)*
   c. ☐ Statement Regarding Federally-sponsored Research/Development *(if applicable)*
   d. ☐ Reference to Microfiche Appendix *(if applicable)*
   e. ☒ Background of the Invention
   f. ☒ Brief Summary of the Invention
   g. ☒ Brief Description of the Drawings *(if drawings filed)*
   h. ☒ Detailed Description
   i. ☒ Claim(s) as Classified Below
   j. ☒ Abstract of the Disclosure

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Application Elements (Continued)

3. ☒ Drawing(s) *(when necessary as prescribed by 35 USC 113)*

   a. ☐ Formal b. ☒ Informal Number of Sheets **One (1)**

4. ☒ Oath or Declaration

   a. ☒ Newly executed *(original or copy)* ☐ Unexecuted

   b. ☐ Copy from a prior application (37 CFR 1.63(d)) *(for continuation/divisional application only)*

   c. ☒ With Power of Attorney ☐ Without Power of Attorney

   d. ☐ *DELETION OF INVENTOR(S)*
   Signed statement attached deleting inventor(s) named in the prior application, see 37 C.F.R. 1.63(d)(2) and 1.33(b).

5. ☐ Incorporation By Reference *(usable if Box 4b is checked)*
The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

6. ☐ Computer Program in Microfiche

7. ☐ Genetic Sequence Submission *(if applicable, all must be included)*

   a. ☐ Paper Copy

   b. ☐ Computer Readable Copy

   c. ☐ Statement Verifying Identical Paper and Computer Readable Copy

Accompanying Application Parts

8. ☒ Assignment Papers *(cover sheet & documents)*

9. ☐ 37 CFR 3.73(b) Statement *(when there is an assignee)*

10. ☐ English Translation Document *(if applicable)*

11. ☐ Information Disclosure Statement/PTO-1449 ☐ Copies of IDS Citations

12. ☐ Preliminary Amendment

13. ☒ Acknowledgment postcard

14. ☐ Certificate of Mailing

   ☐ First Class ☒ Express Mail *(Specify Label No.):* **EJ056023095US**

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Accompanying Application Parts (Continued)

15. ☐ Certified Copy of Priority Document(s) *(if foreign priority is claimed)*

16. ☒ Small Entity Statement(s) - Specify Number of Statements Submitted: **One (1)**

17. ☒ Additional Enclosures *(please identify below):*

Check No. 5712

Fee Calculation and Transmittal

CLAIMS AS FILED

For	#Filed	#Allowed	#Extra	Rate	Fee
Total Claims	13	- 20 =	0	x $9.00	$0.00
Indep. Claims	4	- 3 =	1	x $39.00	$39.00
Multiple Dependent Claims (check if applicable) ☐					$0.00
				BASIC FEE	$380.00
OTHER FEE *(specify purpose)*		Assignment Recording Fee			$40.00
				TOTAL FILING FEE	$459.00

☒ A check in the amount of **$459.00** to cover the filing fee is enclosed.

☒ The Commissioner is hereby authorized to charge and credit Deposit Account No. **19-3795** as described below. A duplicate copy of this sheet is enclosed.

- ☐ Charge the amount of as filing fee.
- ☒ Credit any overpayment.
- ☒ Charge any additional filing fees required under 37 C.F.R. 1.16 and 1.17.
- ☐ Charge the issue fee set in 37 C.F.R. 1.18 at the mailing of the Notice of Allowance, pursuant to 37 C.F.R. 1.311(b).

Dated: **June 25, 1999**

Signature

Gerald W. Spinks
Reg. No. 32,843
P. O. Box 10158
College Station, TX 77842-0158
(409)690-8008

cc:

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) AND 1.27 (c)) - SMALL BUSINESS CONCERN	Docket No. CRYO/US-24

Serial No.	Filing Date	Patent No.	Issue Date

Applicant/ Patentee: **Hong Li**

Invention: **PRECOOLED CRYOGENIC ABLATION SYSTEM**

I hereby declare that I am:

- ☐ the owner of the small business concern identified below:
- ☒ an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN: **CryoGen, Inc.**

ADDRESS OF CONCERN: **11065 Sorrento Valley Court, San Diego, CA 92121**

I hereby declare that the above-identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under Section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the above identified invention described in:

- ☒ the specification filed herewith with title as listed above.
- ☐ the application identified above.
- ☐ the patent identified above.

If the rights held by the above-identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed on the next page and no rights to the invention are held by any person, other than the inventor, who could not qualify as an independent inventor under 37 CFR 1.9(c) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey, or license any rights in the invention is listed below:

☒ no such person, concern or organization exists.
☐ each such person, concern or organization is listed below.

FULL NAME _____
ADDRESS _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

FULL NAME _____
ADDRESS _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

FULL NAME _____
ADDRESS _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

FULL NAME _____
ADDRESS _____

☐ Individual ☐ Small Business Concern ☐ Nonprofit Organization

Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: **David Murray**

TITLE OF PERSON SIGNING OTHER THAN OWNER: **President**

ADDRESS OF PERSON SIGNING: **11065 Sorrento Valley Court, San Diego, CA 92121**

SIGNATURE: David R. Murray DATE: 6/15/99

Express Mail Label No. EJ056023095US

Docket No. CRYO/US-24

PATENT

UNITED STATES PATENT APPLICATION

of

Hong Li

for

PRECOOLED CRYOGENIC ABLATION SYSTEM

TITLE OF THE INVENTION

Precooled Cryogenic Ablation System

CROSS REFERENCE TO RELATED APPLICATIONS

Not Applicable

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

Not Applicable

BACKGROUND OF THE INVENTION

Field of the Invention - This invention is in the field of cooling biological tissues to very low temperatures, for treatment of medical conditions, as in cryosurgery.

Background Information - It is desirable to be able to selectively cool miniature discrete portions of biological tissue to very low temperatures in the performance of cryosurgery, without substantially cooling adjacent tissues of the organ. Cryosurgery has become an important procedure in medical, dental, and veterinary fields. Particular success has been experienced in the specialties of gynecology and dermatology. Other specialties, such as neurosurgery and urology, could also benefit from the implementation of cryosurgical techniques, but this has only occurred in a limited way. Unfortunately, currently known cryosurgical instruments have several limitations which make their use difficult or impossible in some such fields. Specifically, known systems can not achieve the necessary temperature and cooling power to optimally perform cryosurgical ablation, such as in cardiac ablation to correct arrhythmia.

In the performance of cryosurgery, it is typical to use a cryosurgical application system designed to suitably freeze the target tissue, thereby destroying diseased or degenerated cells in the tissue. The abnormal cells to be destroyed are often surrounded by healthy tissue which must be left uninjured. The particular probe, catheter, or other applicator used in a given application is therefore designed with the optimum shape, size, and flexibility or rigidity for the application, to achieve this selective freezing of tissue.

Where a probe or catheter is used, the remainder of the refrigeration system must be designed to provide adequate cooling, which involves lowering the operative portion of the probe to a desired temperature, and having sufficient power or capacity to maintain the desired temperature for a given heat load. The entire system must be designed to place the operative portion of the probe or catheter at the location of the tissue to be frozen, without having any undesirable effect on other organs or systems.

It is an object of the present invention to provide a method and apparatus for precooling a primary loop high pressure refrigerant to a point below its critical temperature, to liquefy the primary refrigerant, with a secondary loop refrigeration cycle. This allows the use of a liquid primary refrigerant having a critical temperature below the operating room temperature, in order to achieve the lower temperature possible with such a primary refrigerant.

BRIEF SUMMARY OF THE INVENTION

The present invention comprises a miniature refrigeration system, including a method for operating the system, including precooling of the primary high pressure refrigerant below its critical temperature, to liquefy the primary refrigerant, with a secondary refrigeration cycle using a second refrigerant with a higher critical temperature, to maximize the available cooling power of the primary refrigerant, and to achieve the lowest possible temperature.

The cooling power is an important design parameter of a cryosurgical instrument. With greater cooling power, more rapid temperature decreases occur, and lower temperatures can be maintained at the probe tip during freezing. This ultimately leads to greater tissue destruction. The power of a J-T cryosurgical device is a function of the enthalpy difference of the primary refrigerant and the mass flow rate. Pre-cooling a refrigerant below its critical temperature and liquefying the refrigerant will increase the enthalpy difference available for cooling power.

An example of a suitable primary refrigerant is SUVA-95, a mixture of R-23 and R-116 refrigerants made by DuPont Fluoroproducts, of Wilmington, Delaware. SUVA-95 has a critical temperature of 287K, with cooling capacity at temperatures as low as 185K at one

atmosphere. An example of a suitable secondary refrigerant is AZ-20, an R-410a refrigerant made by Allied Signal of Morristown, New Jersey. AZ-20 has a critical temperature of 345K, with cooling capacity at temperatures as low as 220K at one atmosphere.

The high pressure primary refrigerant is fed as a gas into a high pressure passageway within a primary-to-secondary heat exchanger. The primary-to-secondary heat exchanger can be a coiled tube heat exchanger or a finned tube heat exchanger. The liquid secondary refrigerant is vaporized and expanded into a low pressure passageway in the primary-to-secondary heat exchanger. Heat exchange between the low pressure secondary refrigerant vapor and the high pressure primary refrigerant cools and liquefies the high pressure refrigerant. The liquid high pressure primary refrigerant is then vaporized and expanded at the cooling tip of a cryosurgical catheter to provide the cooling power necessary for effective ablation of tissue. The method and apparatus of the present invention can be used equally well in a rigid hand held cryoprobe, or in a catheter.

The primary-to-secondary heat exchanger is part of the secondary refrigeration system, which can have a secondary compressor and a secondary expansion element, in addition to the primary-to-secondary heat exchanger. The liquid high pressure secondary refrigerant, having a higher critical temperature than the primary refrigerant, can be at a temperature which is relatively higher than the critical temperature of the primary refrigerant. However, the vaporized and expanded low pressure secondary refrigerant is at a temperature which is low enough to cool the primary refrigerant below its critical temperature. Since the secondary refrigerant has a critical temperature above normal operating room temperature, it can easily be provided in the liquid state in an operating room environment, whereas the primary refrigerant, which has a critical temperature significantly below normal operating room temperature, can not.

The liquid high pressure primary refrigerant is conducted from the heat exchanger to the inlet of a primary Joule-Thomson expansion element located in the cold tip of the probe or catheter, where the primary refrigerant is vaporized and expanded to a lower pressure and a lower temperature.

The primary refrigerant exiting the primary Joule-Thomson expansion element is exposed to the inner surface of a heat transfer element at the cold tip. The vaporized and

expanded primary refrigerant cools the heat transfer element to a lower temperature and then returns through the low pressure return passageway of the catheter or probe.

The novel features of this invention, as well as the invention itself, will be best understood from the attached drawings, taken along with the following description, in which similar reference characters refer to similar parts, and in which:

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

Figure 1 is a schematic view of the preferred embodiment of the apparatus of the present invention; and

Figure 2 is a schematic section view of the primary-to-secondary heat exchanger used in the apparatus shown in Figure 1.

DETAILED DESCRIPTION OF THE INVENTION

The present invention lies in the appropriate use of a secondary evaporative refrigeration system to precool and liquefy the primary high pressure refrigerant, before passage of the primary refrigerant through a primary Joule-Thomson expansion element. This is intended to enable the generation of a sufficiently low temperature, and to maximize the available cooling power, at the cold tip of a cryosurgical probe or catheter.

Pre-cooling the primary refrigerant to an at least partially liquid state, prior to feeding it to the primary expansion element, is the focus of the present invention. This pre-cooling can be done prior to introducing the primary refrigerant into the catheter, by the use of a heat exchanger in a cooling console. Alternatively, pre-cooling can be provided nearer to the treatment area, such as in the handle of a cryoprobe, or at the proximal end of a catheter.

An important parameter in the design of a cryosurgical device is the cooling power which the refrigeration system can develop. The cooling power determines the rate of cooling in degrees per second, and the temperature which can be maintained at the probe tip during freezing of the tissue. The rate of freezing is important in achieving cell death, since more rapid freezing results in better formation of intracellular ice crystals, resulting in cell lysis. The rate of freezing also determines the length of time required to perform a given

procedure on the patient. The quicker the procedure, the less traumatic the procedure is to the patient.

The temperature which can be maintained at the probe cold tip determines the size of the ice ball formed in the surrounding tissue. This, of course, determines the total volume of tissue destroyed at each location, and the speed with which the procedure can be completed.

In Joule-Thomson cryosurgical devices, high pressure fluid expands across a restriction of some kind, such as a small orifice, or a restricted tube. The sudden drop in pressure results in a corresponding drop in temperature. The cooling power of the device is the product of the mass flow rate of the cryogen and the enthalpy difference at the different pressures and temperatures. The flow rate is a function of orifice size and the temperature and pressure of the cryogen. For a given orifice size, under non-choking conditions, the density of the cryogen is higher at higher pressures and lower temperatures, resulting in a higher mass flow rate. The maximum flow rate is found at the point where the cryogen is a liquid. The enthalpy difference is also a function of the pressure and temperature. For a given temperature and a given pressure, the maximum enthalpy difference between two conditions occurs at the liquefaction point of the cryogen. Incorporating a pre-cooling heat exchanger into the refrigeration system, to promote liquefaction of the high pressure primary cryogen, increases the power of the system.

If the primary refrigerant is in the gaseous state upon startup of the refrigeration system, the early flow rate is very low, and the power is very low. Therefore, the initial cool down is very slow at overcoming the low flow rate. Further, the cold tip is typically placed within the patient, and in contact with the target tissue, before commencement of cooldown, placing a significant heat load on the tip. This means that cooldown can be unacceptably slow, and in some cases, it may not occur at all.

In order to maximize the performance of the present cryosurgical system, and to eliminate the problems normally associated with slow cooldown rates and low cooling power, an independent secondary evaporative refrigeration system is incorporated. The primary system uses a refrigerant such as freon, or SUVA-95, to achieve the desired temperature and capacity at the cold tip. However, the critical temperature of such a refrigerant is below the temperature normally found in the operating room environment, so

provision of the primary refrigerant in the liquid state requires precooling. The secondary system uses a refrigerant such as AZ-20, to pre-cool and liquefy the primary refrigerant prior to flow of the primary refrigerant to the cold tip. The secondary system accomplishes this pre-cooling through a primary-to-secondary heat exchanger. This pre-cooling causes the initial flow rate and the cooling power of the system to be higher, making the initial cooldown rate much faster.

As shown in Figure 1, the apparatus 10 of the present invention includes a source of gaseous high pressure primary refrigerant 12, a source of liquid high pressure secondary refrigerant 14, a primary-to-secondary heat exchange unit 16, and a probe or catheter 18 with a cold tip 20. The gaseous primary refrigerant source 12 can incorporate a pressure bottle as schematically shown, with the primary loop being an open loop, or the source 12 can incorporate a compressor, with the primary loop being a closed loop, as will be explained below. The primary refrigerant is one which, in order to deliver the desired temperature and cooling capacity at the cold tip 20, necessarily has a critical temperature below the temperature of the operating room environment. The purpose of the present invention is to cool that gaseous pimary refrigerant below its critical temperature and convert it to a liquid refrigerant, in order to achieve the desired temperature and cooling capacity. A flexible coaxial catheter 18 can be constructed with an outer tube made of pebax, and an inner tube made of polyimide.

Gaseous high pressure primary refrigerant flows from the primary refrigerant source 12 via a conduit 32 into the heat exchange unit 16. After heat exchange and liquefaction, liquid primary refrigerant, at a temperature below the temperature of the operating room environment, flows from the heat exchange unit 16 into the catheter or probe 18. Near the distal tip of the catheter 18, the liquid primary refrigerant is vaporized and expanded at an expansion element shown schematically as an orifice 36. This lowers the temperature of the primary refrigerant to the desired temperature, enabling the refrigerant to cool the cold tip 20 to the selected temperature for tissue ablation. Gaseous primary refrigerant returning from the cold tip 20 exits the heat exhange unit 16 via a conduit 34. Where the primary refrigerant source 12 incorporates a pressure bottle, the primary loop can be operated as an open loop, and the gaseous primary refrigerant conduit 34 can be collected by a compressor

22 to vent to atmosphere or to a collector 24. Alternatively, the primary loop can be operated as a closed loop, and the gaseous primary refrigerant conduit 32 can be routed (not shown) from the outlet of the compressor 22, as is well know in the art.

The liquid secondary refrigerant source 14 can incorporate a compressor unit as schematically shown, or it can incorporate a pressure bottle. If required to generate the necessary pressure for liquefaction of the secondary refrigerant, a compressor can be used to raise the pressure of the effluent from a pressure bottle. The secondary refrigerant source 14 can also include a condensor, as is well known in the art, for liquefying the secondary refrigerant, if required. The secondary refrigerant must be one which has a critical temperature above the temperature of the operating room environment, so that the secondary refrigerant can be conducted in liquid form to the primary-to-secondary heat exchange unit 16. This enables the use of the phase-change enthalpy difference in the secondary refrigerant to provide the necessary cooling to take the primary refrigerant below its critical temperature in the heat exchange unit 16.

Liquid high pressure secondary refrigerant, at a temperature above the temperature of the operating room environment, flows from the secondary refrigerant source 14 via a conduit 28 into the heat exchange unit 16. After vaporization and heat exchange, gaseous secondary refrigerant flows from the heat exchange unit 16 via a conduit 30. Where the secondary refrigerant source 14 incorporates a pressure bottle, the secondary loop can be operated as an open loop, and the gaseous secondary refrigerant conduit 30 can vent to atmosphere or to a collector (not shown) as is well known in the art. Alternatively, the secondary loop can be operated as a closed loop, and the gaseous secondary refrigerant conduit 30 can be routed to the inlet of a compressor in the secondary refrigerant source 14, as shown.

As shown schematically in Figure 2, liquid high pressure secondary refrigerant enters the heat exchange unit 16 via a supply conduit 28 and is vaporized and expanded via a secondary expansion element shown as a capillary tube 29. The vaporized and expanded secondary refrigerant, at a temperature below the critical temperature of the primary refrigerant, then flows through a secondary refrigerant flow path in a primary-to-secondary heat exchanger 26 and exits the heat exchange unit 16 via a return conduit 30.

Gaseous high pressure primary refrigerant enters the heat exchange unit 16 via a supply conduit 32 and flows through a primary refrigerant flow path in the heat exchanger 26. Since the temperature of the secondary refrigerant flowing through the heat exchanger 26 is significantly below the critical temperature of the primary refrigerant, the primary refrigerant is liquefied in the heat exchanger 26. Liquid primary refrigerant then exits the heat exchanger via a conduit 33 and flows through the catheter 18 to a primary expansion element, shown schematically as an orifice 36, near the cold tip 20. The primary expansion element 36 vaporizes and expands the primary refrigerant to the selected temperature for cooling the cold tip 20 to the desired temperature for ablation of tissue. The vaporized and expanded primary refrigerant returning from the cold tip 20 then flows back through the catheter 18, through the heat exchange unit 16, and exits the heat exchange unit 16 via a return conduit 34.

While the particular invention as herein shown and disclosed in detail is fully capable of obtaining the objects and providing the advantages hereinbefore stated, it is to be understood that this disclosure is merely illustrative of the presently preferred embodiments of the invention and that no limitations are intended other than as described in the appended claims.

CLAIMS

I claim:

1. A cryosurgical instrument for ablation of endocardiac tissue, comprising:

a source of a gaseous primary refrigerant, said source providing said primary refrigerant at a temperature above the critical temperature of said primary refrigerant;

a source of a liquid secondary refrigerant, said secondary refrigerant having a critical temperature higher than said critical temperature of said primary refrigerant;

a secondary expansion element connected to receive said liquid secondary refrigerant, said secondary expansion element being constructed to vaporize and expand said secondary refrigerant to a temperature below said critical temperature of said primary refrigerant;

a primary-to-secondary heat exchanger having a primary refrigerant flow path connected to receive said gaseous primary refrigerant, and a secondary refrigerant flow path connected to receive said vaporized and expanded secondary refrigerant from said secondary expansion element, said heat exchanger being constructed to cool and liquefy said primary refrigerant;

a primary expansion element connected to receive said liquid primary refrigerant from said heat exchanger, said primary expansion element being constructed to vaporize and expand said primary refrigerant to a selected cryogenic temperature; and

a cryoablation heat transfer element connected to receive said vaporized and expanded primary refrigerant.

2. A cryosurgical instrument as recited in claim 1, further comprising a flexible coaxial catheter connected at a proximal end to said primary-to-secondary heat exchanger, said coaxial catheter having an outer low pressure tube and an inner high pressure tube, said primary expansion element and said heat transfer element being located near a distal end of said flexible catheter.

3. A cryosurgical instrument as recited in claim 2, wherein:

said outer tube of said coaxial catheter is constructed of pebax polymer; and

said inner tube of said coaxial catheter is constructed of polyimide polymer.

4. A cryosurgical instrument as recited in claim 1, further comprising a compressor unit connected to receive said gaseous secondary refrigerant from said heat exchanger and to repressurize, liquefy, and return said secondary refrigerant to said secondary expansion element.

5. A cryosurgical instrument as recited in claim 1, further comprising a vent path connected to receive said gaseous secondary refrigerant from said heat exchanger.

6. A cryosurgical instrument as recited in claim 1, further comprising a compressor unit connected to collect said gaseous primary refrigerant returning from said heat transfer element.

7. A cryosurgical instrument as recited in claim 1, further comprising a vent path connected to receive said gaseous primary refrigerant returning from said heat transfer element.

8. A cryosurgical instrument as recited in claim 1, wherein said primary refrigerant has a critical temperature below about 22° C, and said secondary refrigerant has a critical temperature above about 22° C.

9. A cryosurgical instrument as recited in claim 1, wherein said primary refrigerant comprises SUVA-95, and said secondary refrigerant comprises AZ-20.

10. A cryosurgical instrument for ablation of endocardiac tissue, comprising:

a source of a gaseous primary refrigerant, said source providing said primary refrigerant at a temperature above the critical temperature of said primary refrigerant;

a compressor unit constructed to provide a liquid secondary refrigerant, said secondary refrigerant having a critical temperature higher than said critical temperature of said primary refrigerant;

a secondary expansion element connected to receive said liquid secondary refrigerant, said secondary expansion element being constructed to vaporize and expand said secondary refrigerant to a temperature below said critical temperature of said primary refrigerant;

a primary-to-secondary heat exchanger having a primary refrigerant flow path connected to receive said gaseous primary refrigerant, and a secondary refrigerant flow path connected to receive said vaporized and expanded secondary refrigerant from said secondary expansion element, said heat exchanger being constructed to cool and liquefy said primary refrigerant;

a secondary refrigerant return path connected to receive said gaseous secondary refrigerant returning from said heat exchanger and to conduct said gaseous secondary refrigerant to an inlet of said compressor unit;

a primary expansion element connected to receive said liquid primary refrigerant from said heat exchanger, said primary expansion element being constructed to vaporize and expand said primary refrigerant to a selected cryogenic temperature;

a cryoablation heat transfer element connected to receive said vaporized and expanded primary refrigerant;

a flexible coaxial catheter connected at a proximal end to said primary-to-secondary heat exchanger, said coaxial catheter having an outer low pressure tube and an inner high pressure tube, said primary expansion element and said heat transfer element being located near a distal end of said flexible catheter; and

a vent path connected to receive said gaseous primary refrigerant returning from said heat transfer element.

11. A method for cooling a cryoprobe cold tip for ablation of endocardiac tissue, said method comprising:

providing a gaseous primary refrigerant at a temperature above the critical temperature of said primary refrigerant;

providing a liquid secondary refrigerant, said secondary refrigerant having a critical temperature higher than said critical temperature of said primary refrigerant;

providing a primary-to-secondary heat exchanger having a primary refrigerant flow path and a secondary refrigerant flow path;

flowing said gaseous primary refrigerant through said primary refrigerant flow path of said heat exchanger;

flowing said liquid secondary refrigerant through a secondary expansion element to thereby vaporize and expand said secondary refrigerant to a temperature below said critical temperature of said primary refrigerant;

flowing said vaporized and expanded secondary refrigerant from said secondary expansion element through said secondary refrigerant flow path of said heat exchanger to cool and liquefy said primary refrigerant;

flowing said liquid primary refrigerant through a primary expansion element to thereby vaporize and expand said primary refrigerant to a selected cryogenic temperature; and

exposing said cold tip to said vaporized and expanded primary refrigerant.

12. A method as recited in claim 11, further comprising:

compressing and condensing said gaseous secondary refrigerant exiting from said heat exchanger and returning said secondary refrigerant to said secondary expansion element; and

venting said gaseous primary refrigerant exiting from said cold tip.

13. A method for cryogenic ablation of endocardiac tissue, comprising:

providing a primary refrigerant at a temperature above the critical temperature of said primary refrigerant;

providing a liquid secondary refrigerant having a critical temperature higher than said critical temperature of said primary refrigerant;

providing a secondary expansion element, a primary-to-secondary heat exchanger, a flexible catheter, a heat transfer element in the distal tip of said catheter, and a primary expansion element near said heat transfer element;

inserting said flexible catheter into a blood vessel of a patient;

directing said distal tip of said catheter to a desired cardiovascular location;

vaporizing and expanding said secondary refrigerant, with said secondary expansion element, to cool said secondary refrigerant to a temperature below said critical temperature of said primary refrigerant;

cooling and liquefying said primary refrigerant with said vaporized and expanded secondary refrigerant, in said primary-to-secondary heat exchanger;

delivering said cooled and liquefied primary refrigerant to said primary expansion element near said distal tip of said catheter;

vaporizing and expanding said primary refrigerant, with said primary expansion element, to further cool said primary refrigerant; and

cooling said heat transfer element with said vaporized and expanded primary refrigerant.

ABSTRACT OF THE DISCLOSURE

A method and apparatus for using a secondary refrigerant to precool and liquefy a primary refrigerant, then vaporizing and expanding the primary refrigerant to cool a cold tip of a cryosurgical instrument for ablation of biological tissue, such as cardiovascular tissue, in particular endocardiac tissue and tissue inside a cardiac blood vessel. The secondary refrigerant has a critical temperature above the critical temperature of the primary refrigerant, and a cooling temperature below the critical temperature of the primary refrigerant, thereby facilitating the use of the precooling step to provide liquid primary refrigerant in an operating room environment in which the primary refrigerant could not otherwise be provided in the liquid phase.

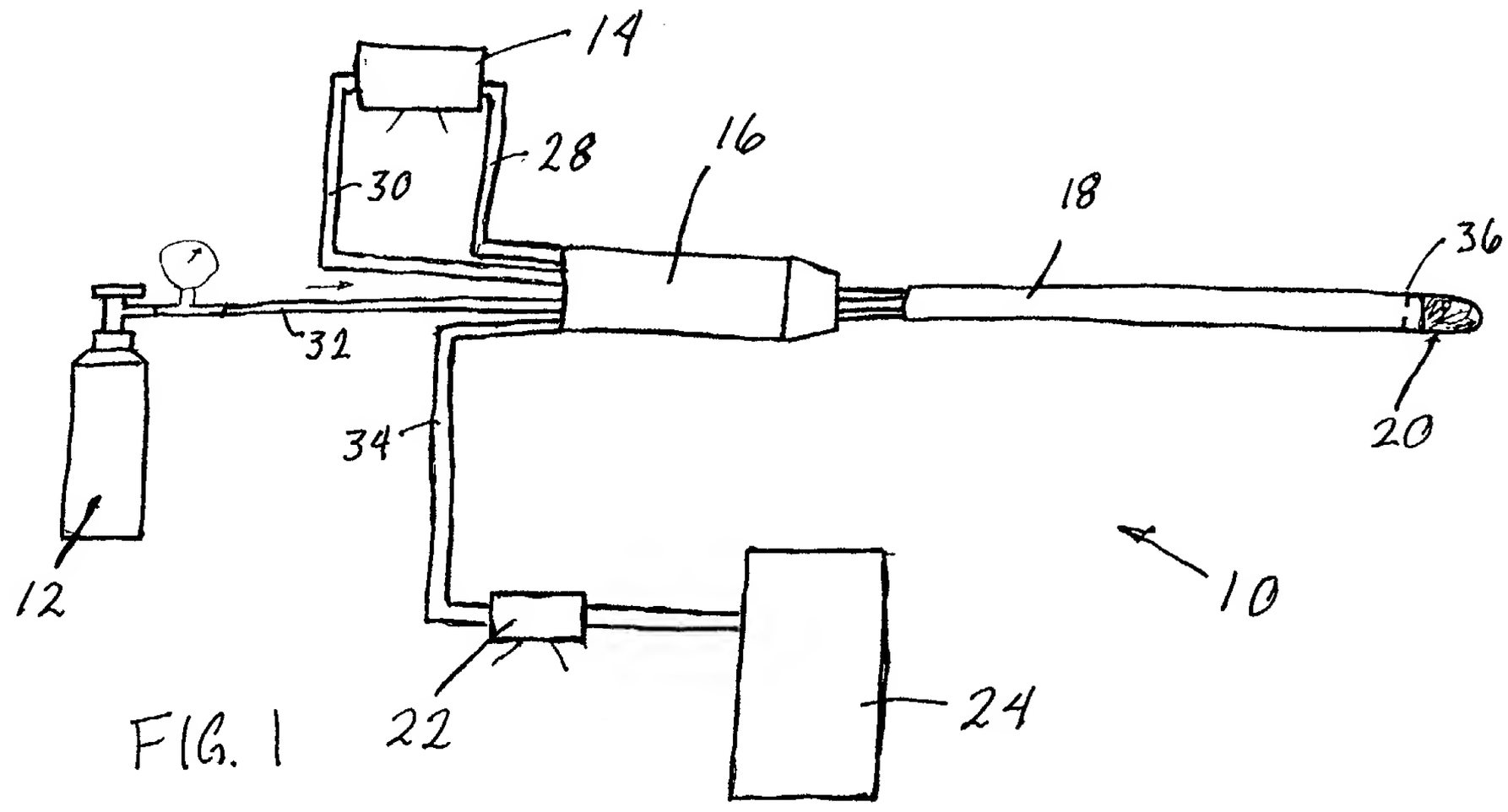

FIG. 1

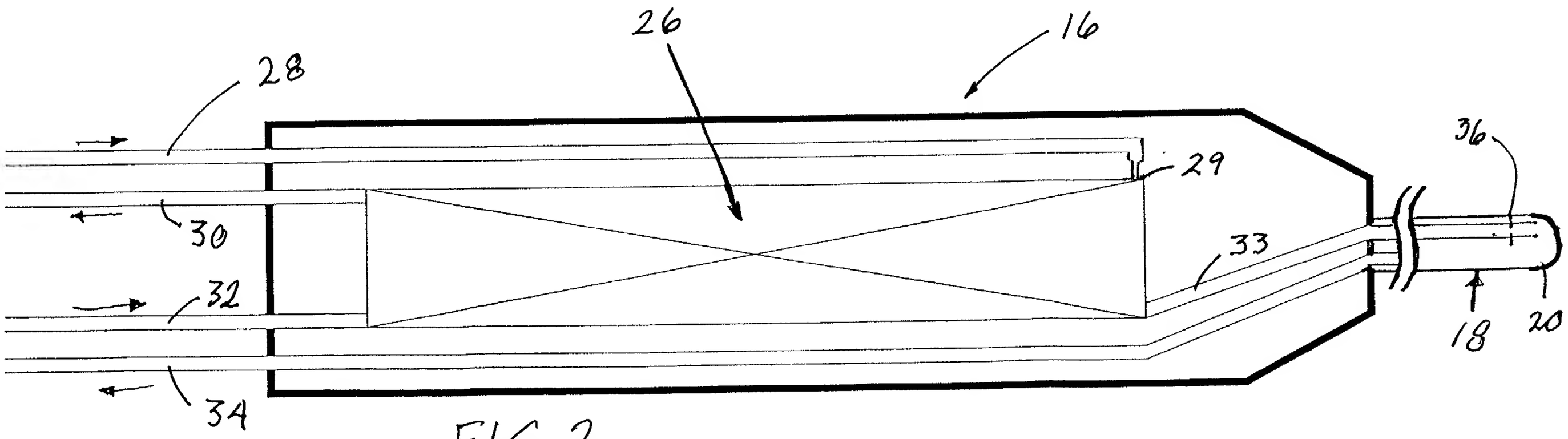

FIG. 2

Docket No.
CRYO/US-24

Declaration and Power of Attorney For Patent Application

English Language Declaration

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

PRECOOLED CRYOGENIC ABLATION SYSTEM

the specification of which

(check one)

☒ is attached hereto.

☐ was filed on _____ as United States Application No. or PCT International Application Number _____

and was amended on _____

(if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, Section 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, Section 119(a)-(d) or Section 365(b) of any foreign application(s) for patent or inventor's certificate, or Section 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate or PCT International application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s)			Priority Not Claimed
None			☐
(Number)	(Country)	(Day/Month/Year Filed)	
			☐
(Number)	(Country)	(Day/Month/Year Filed)	
			☐
(Number)	(Country)	(Day/Month/Year Filed)	

I hereby claim the benefit under 35 U.S.C. Section 119(e) of any United States provisional

None	
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)
(Application Serial No.)	(Filing Date)

I hereby claim the benefit under 35 U. S. C. Section 120 of any United States application(s), or Section 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of 35 U.S.C. Section 112, I acknowledge the duty to disclose to the United States Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, C. F. R., Section 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

None		
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)
(Application Serial No.)	(Filing Date)	(Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. *(list name and registration number)*

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Second inventor's signature Date
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Citizenship
Post Office Address